

AMENDMENT OF CLAIMS

1. A medicinal or pharmaceutical composition(s) for promoting the expression of a cell death-suppressing gene product Bcl-x_L comprising ginseng, its extracts, ginseng components, metabolites thereof or salts thereof.
2. (Amended) A medicinal or pharmaceutical composition(s) for suppressing apoptosis or apoptosis-like cell death of brain cells, nerve cells, neural stem cells, glial cells, vascular endothelial cells, vascular smooth muscle cells, hepatocytes liver cells, Kupffer's cells, sinusoid endothelial cells, fibroblasts, biliary epithelial cells, lipocytes, lymphocytes, leukocytes, reticulum cells, macrophages or plasma cells, comprising ginseng, its extracts, ginseng components, metabolites thereof or salts thereof, in which the extracellular fluid concentrations of the said composition(s) in lesioned tissues are adjusted to 14.5 ng/ml or less.
3. The medicinal or pharmaceutical composition(s) according to claim 1 or claim 2 wherein the ginseng extracts are the extracts of ginseng.
4. The medicinal or pharmaceutical composition(s) according to claim 1 or claim 2 wherein the ginseng or its extracts are red ginseng powder or its extracts.
5. The medicinal or pharmaceutical composition(s) according

to claim 1 or claim 2 wherein ginseng components, metabolites thereof or salts thereof are crude saponin fractions, non-saponin fractions, purified saponins, constituents of saponin fractions or salts thereof.

6. The medicinal or pharmaceutical composition(s) according to any one of claims 1 - 5 wherein tissues in promoting the expression of a cell death-suppressing gene product Bcl-x_L are the brain and nervous tissues or the spinal cord tissues.

7. The medicinal or pharmaceutical composition(s) according to any one of claims 1 - 5 wherein tissues in promoting the expression of a cell death-suppressing gene product Bcl-x_L are the liver or the spleen.

8. (Cancelled)

9. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 2 - 5 for therapy, prevention or treatment of diseases causing apoptosis or apoptosis-like cell death of cells according to claim 2.

10. The medicinal or pharmaceutical composition(s) according to any one of claims 1 - 5 for therapy, prevention or treatment of brain and nervous diseases.

11. The medicinal or pharmaceutical composition(s) according to claim 10 wherein the brain and nervous diseases are cerebrovascular dementia, cerebral infarction or cerebral apoplexy.

12. The medicinal or pharmaceutical composition(s) according to any one of claims 1 - 11 comprising preparations for oral administration.
13. The medicinal or pharmaceutical composition(s) according to claim 12 wherein amount of administration for mammals is 1/6 - 1/2 g/kg in a day.
14. The medicinal or pharmaceutical composition(s) according to any one of claims 1 - 11 comprising preparations for intravenous administration.
15. The medicinal or pharmaceutical composition(s) according to claim 14 comprising preparations for single intravenous administration or preparations for repetitive or continuous intravenous administration.
16. (Cancelled)
17. (Amended) A preparation(s) for intravenous administration according to any one of claims 12 - 15 wherein the extracellular fluid concentrations of ginseng, its extracts, ginseng components, metabolites thereof or salts thereof in lesioned tissues are 1 - 1450 fg/ml or 1 - 145000 fg/ml.
18. (Amended) A medicinal or pharmaceutical composition(s) for therapy, prevention or treatment of diseases caused by injuries to the nervous tissues or spinal cord tissues comprising ginseng, its extracts, ginseng components, metabolites thereof or salts thereof, in which the

extracellular fluid concentrations of the said composition(s) in lesions are adjusted to 14.5 ng/ml or less.

19. The medicinal or pharmaceutical composition(s) according to claim 18 wherein the ginseng extracts are the extracts of ginseng.

20. The medicinal or pharmaceutical composition(s) according to claim 18 wherein the ginseng or its extracts are red ginseng powder or its extracts.

21. The medicinal or pharmaceutical composition(s) according to claim 18 wherein ginseng components, metabolites thereof or salts thereof are crude saponin fractions, non-saponin fractions, purified saponins, constituents of saponin fractions or salts thereof.

22. (Cancelled)

23. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 21 wherein the concentrations of ginseng, its extracts, ginseng components, metabolites thereof or salts thereof are 1 - 1450 fg/ml or 1 - 145000 fg/ml.

24. The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 23 comprising preparations for intravenous administration.

25. The medicinal or pharmaceutical composition(s) according to claim 24 comprising preparations for single intravenous

administration or preparations for repetitive or continuous intravenous administration.

26. (Cancelled)

27. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein the diseases caused by injuries to the nervous tissues or spinal cord tissues are spinal cord injuries.

28. (Amended) The medicinal or pharmaceutical composition(s) according to claim 27 comprising improving paralysis of upper extremities or lower extremities.

29. (Amended) The medicinal or pharmaceutical composition(s) according to claim 27 comprising improving urination disorder or dyschezia.

30. (Amended) The medicinal or pharmaceutical composition(s) according to claim 27 comprising improving neurogenic bladder.

31. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein diseases caused by injuries to the nervous tissues or spinal cord tissues are secondary degeneration of the nervous tissues.

32. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein diseases caused by injuries to the nervous tissues or spinal cord tissues are trauma to the nervous tissues or the spinal

cord tissues.

33. The medicinal or pharmaceutical composition(s) according to claim 32 wherein trauma is spinal cord injuries, neurotrauma or head injuries.

34. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein diseases caused by injuries to the nervous tissues or spinal cord tissues are diseases caused by apoptosis or apoptosis-like cell death of oligodendrocytes.

35. The medicinal or pharmaceutical composition(s) according to claim 34 wherein diseases causing apoptosis or apoptosis-like cell death of oligodendrocytes are spinal cord injuries.

36. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein diseases caused by injuries to the nervous tissues or spinal cord tissues are demyelination.

37. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein diseases caused by injuries to the nervous tissues or spinal cord tissues are brain edema, brain and nervous tissue edema or spinal tissue edema.

38. (Amended) The medicinal or pharmaceutical composition(s) according to claim 37 wherein diseases causing

brain edema, brain and nervous tissue edema or spinal cord tissue edema are cerebral hemorrhage, subarachnoidal hemorrhage, head injuries, spinal cord injuries or neurotrauma.

39. (Amended) The medicinal or pharmaceutical composition(s) according to any one of claims 18 - 25 wherein diseases caused by injuries to the nervous tissues or spinal cord tissues are spinal cord injuries, head injuries or neurotrauma.

40. (Amended) A medicinal or pharmaceutical composition(s) for therapy, prevention or treatment of cardiac diseases comprising ginseng, its extracts, ginseng components, metabolites thereof or salts thereof, in which the extracellular fluid concentrations of the said composition(s) in lesioned tissues are adjusted to 14.5 ng/ml or less.

41. The medicinal or pharmaceutical composition(s) according to claim 40 wherein cardiac diseases are accompanied with apoptosis of myocardial cells or apoptosis-like myocardial cell death.

42. The medicinal or pharmaceutical composition(s) according to claim 5 or claim 21 wherein any one of the constituents of saponin fractions of ginseng is ginsenoside Rb₁.

43. (Cancelled)

44. (Amended) A preparation(s) for intravenous administration comprising containing low concentratoins of

ginseng, its extracts, ginseng components, metabolites thereof or salts thereof.

45. The preparation(s) for intravenous administration according to claim 44 wherein the extracellular fluid concentrations of ginseng, its extracts, ginseng components, metabolites thereof or salts thereof in lesioned tissues are adjusted to 1 ng/ml or less.

46. The preparation(s) for intravenous administration according to claim 45 wherein the extracellular fluid concentrations of ginseng, its extracts, ginseng components, metabolites thereof or salts thereof in lesioned tissues are 1 - 100 fg/ml or 1 - 10000 fg/ml.

47. (Amended) The preparation(s) for intravenous administration according to any one of claims 44 - 46 comprising treating, preventing or curing brain and nervous diseases.

48. (Amended) The preparation(s) for intravenous administration according to claim 47 wherein the brain and nervous diseases are spinal cord injuries, head injuries, neurotrauma, cerebrovascular dementia, cerebral infarction, cerebral apoplexy or transient cerebral ischemic attack.

49. (Amended) The preparation(s) for intravenous administration according to any one of claims 44 - 46 comprising treating, preventing or curing cardiac diseases.

50. The preparation(s) for intravenous administration

according to claim 49 wherein cardiac diseases are accompanied with apoptosis of myocardial cells or apoptosis-like myocardial cell death.

51. (Amended) The preparation(s) for intravenous administration according to any one of claims 44 - 50 comprising preparations for single intravenous administration or preparations for repetitive or continuous intravenous administration.

52. (Amended) A protective agent(s) for brain cells, nerve cells or myocardial cells comprising the preparation(s) for intravenous administration according to any one of claims 44 - 51.

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myocardial cells comprising the preparation(s) for intravenous administration according to any one of claims 43 - 51.

53. A medicinal or pharmaceutical composition(s) for preventing, treating, curing or reducing edema(ta) of biological tissues or living tissues comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

54. The medicinal or pharmaceutical composition(s) according to claim 53 wherein edema(ta) of the biological tissues or living tissues is brain edema, brain and nervous tissue edema or spinal cord tissue edema.

55. The medicinal or pharmaceutical composition(s) according to claim 54 wherein diseases causing brain edema, brain and nervous tissue edema or spinal cord tissue edema are cerebral apoplexy, cerebral infarction, cerebral hemorrhage, subarachnoidal hemorrhage, head injuries, spinal cord injuries or neurotrauma.

56. A medicinal or pharmaceutical composition(s) for prevention, treatment or therapy of bedsore(decubitus) comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

57. The medicinal or pharmaceutical composition(s) according to claim 56 wherein bedsore(decubitus) is caused by spinal cord injuries.

58. A medicinal or pharmaceutical composition(s) for prevention, treatment or therapy of neuroparalysis comprising

ginsenoside Rb₁, metabolites thereof or salts thereof.

59. The medicinal or pharmaceutical composition(s) according to claim 58 wherein neuroparalysis is paraplegia of the upper extremities or lower extremities after spinal cord injuries.

60. A medicinal or pharmaceutical composition(s) for prevention, treatment or therapy of urination disorder or dyschezia comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

61. The medicinal or pharmaceutical composition(s) according to claim 60 wherein urination disorder or dyschezia is caused by spinal cord injuries.

62. A medicinal or pharmaceutical composition(s) for prevention, treatment or therapy of neurogenic bladder comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

63. The medicinal or pharmaceutical composition(s) according to claim 62 wherein neurogenic bladder is caused by spinal cord injuries.

64. A medicinal or pharmaceutical composition(s) for promoting the expression of a cell death-suppressing gene product Bcl-x_L in oligodendrocytes comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

65. A protective agent(s) for oligodendrocytes comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

66. A medicinal or pharmaceutical composition(s) for

suppressing apoptosis or apoptosis-like cell death of myocardial cells comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

67. A medicinal or pharmaceutical composition(s) for promoting the expression of a cell death-suppressing gene product Bcl-x_L in myocardial cells comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

68. The medicinal or pharmaceutical composition(s) according to claim 66 or claim 67 comprising treating, preventing or curing diseases accompanied with cardiac cell death.

69. A protective agent(s) for myocardial cells comprising ginsenoside Rb₁, metabolites thereof or salts thereof.

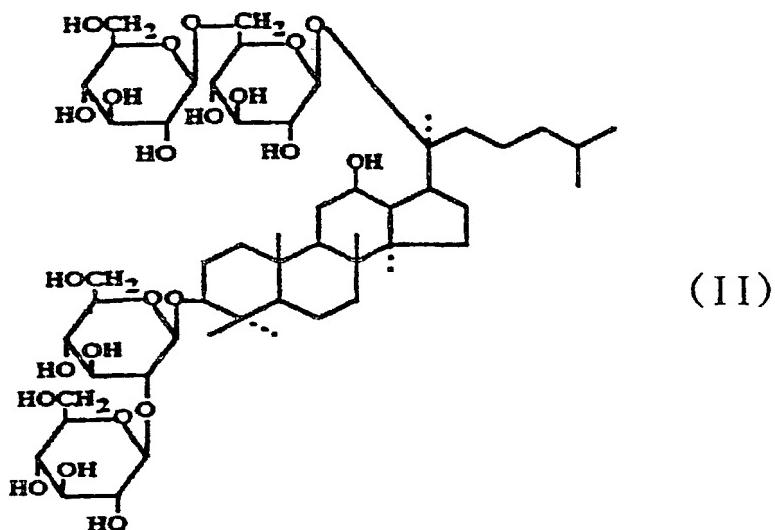
70. The medicinal or pharmaceutical composition(s) according to any one of claims 53 - 69 wherein the extracellular fluid concentrations of ginsenoside Rb₁, metabolites thereof or salts thereof in lesions are 1 ng/ml or less or approximately 0.9 nM or less.

71. The medicinal or pharmaceutical composition(s) according to claim 70 wherein the concentrations of ginsenoside Rb₁, metabolites thereof or salts thereof in lesions are 1 - 100 fg/ml (approximately 0.9 - 90 fM) or 1 - 10⁴ fg/ml (approximately 0.9 - 9000 fM).

72. The medicinal or pharmaceutical composition(s) according to any one of claims 53 - 69 comprising preparations for intravenous administration.

73. The medicinal or pharmaceutical composition(s) according to any one of claims 53 - 69 comprising preparations for single intravenous administration or for repetitive or continuous intravenous administration.

74. Dihydroginsenoside Rb₁ represented by the following formula (II):



or metabolites thereof or salts thereof.

75. A medicinal or pharmaceutical composition(s) comprising the compound according to claim 74, metabolites thereof or salts thereof, for suppressing apoptosis of cells or apoptosis-like cell death.

76. The medicinal or pharmaceutical composition(s) according to claim 75 wherein the cells are brain cells or nerve cells in ischemic penumbra.

77. A medicinal or pharmaceutical composition(s) comprising

the compound according to claim 74, metabolites thereof or salts thereof for therapy, prevention or treatment of brain and nervous diseases.

78. The medicinal or pharmaceutical composition(s) according to claim 77 wherein the brain and nervous diseases are cerebral infarction, cerebral apoplexy or transient cerebral ischemic attack.

79. The medicinal or pharmaceutical composition(s) according to any one of claims 75 - 78 comprising preparations for intravenous administration.

80. The medicinal or pharmaceutical composition(s) according to claim 79 comprising preparations for single intravenous administration or for repetitive or continuous intravenous administration.

81. A method(s) for exploring novel active ingredients or compounds for prevention, treatment or therapy of diseases of the nervous tissues or spinal cord tissues comprising using ginseng, its extracts, ginseng components, metabolites thereof or salts thereof as a leading compounds(s).

82. The method(s) according to claim 81 wherein any one of components contained in saponin fractions of ginseng is ginsenoside Rb₁.

83. The method(s) according to claim 81 or claim 82 wherein the diseases of the nervous tissues or spinal cord tissues are the diseases caused by injuries to the nervous tissues or spinal

- cord tissues or cerebral infarction.
84. An agent(s) for prevention, treatment or therapy of diseases of the nervous tissues or spinal cord tissues, obtained by the method(s) according to any one of claims 81 - 83.
85. Use of any one of constituents of saponin fractions of ginseng or metabolites thereof as a leading compound(s) for exploring novel active ingredients or compounds for prevention, treatment or therapy of diseases of the nervous tissues or spinal cord tissues.
86. Use of any one of constituents of saponin fractions of ginseng or metabolites thereof as a leading compound(s) for exploring an agent(s) for treatment or therapy of neurotrauma, an agent(s) for treatment or therapy of spinal cord injuries, an agent(s) for treatment or therapy of head injuries, a protective agent(s) for brain cells or a protective agent(s) for nerve cells.
87. Use of any one of constituents of saponin fractions of ginseng, metabolites thereof or salts thereof for production of the medicinal or pharmaceutical composition for preventing, treating or curing diseases caused by injuries to the nervous tissues or spinal cord tissues.
88. A method(s) for searching a novel compound(s) having protective actions on brain cells or nerve cells comprising using a component(s) contained in ginseng as a leading compound(s).